Overview of Durham VAMC Human Subject Research Procedures

(Principal Investigator Training)

An Introductory Guide for Investigators and Research Staff

VA Mid-Atlantic Health Care Network

VAMC DURHAM

Version: June, 2018

Overview of Durham VAMC Human Subject Research Procedures

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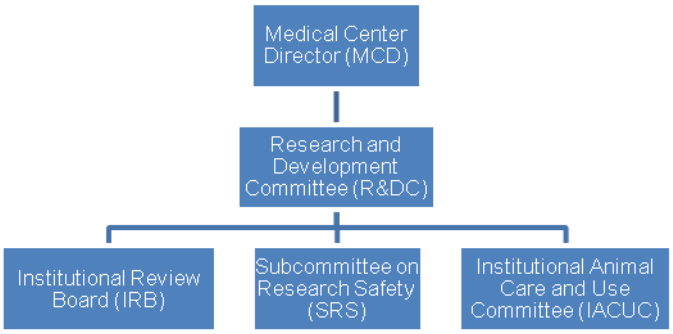
1: Durham VAMC Research Program Structure and Contacts



Research and Development Committee (R&DC):

- Provides overall direction and oversight for the R&D Program.
- Responsible for maintaining high standards for the conduct of quality research and for the welfare of all human research participants, animals and research staff.

Institutional Review Board (IRB):

- Protects the rights and welfare of all research participants in VA-approved research.
- Reviews and approves all VA protocols involving human subjects research prior to initiation and continually monitors ongoing research through periodic reviews at time intervals appropriate to the degree of risk, by review of adverse events (both cumulative and individual), and by review of all proposed modifications affecting human use.

ALL research requires written R&DC approval and Associate Chief of Staff (ACOS-R&D) signature before research can commence.

If the research is human subject research, IRB approval is required and is obtained prior to R&D approval and ACOS-R&D signature. If research is human subject research that involves biological, chemical, physical, or radiation hazards, SRS approval is required and is obtained after IRB approval but before R&D approval and ACOS-R&D signature.

Name	Role	E-mail
Kelvin Pleasent	IRB Administrator	Kelvin.Pleasent@va.gov
Brendlin Green	Program Specialist	Brendlin.Green@va.gov
Courtney Taylor	Program Support	Courtney.Taylor@va.gov
Marion Aldridge	Program Support Assistant	Marion.Aldridge@va.gov
Nancy Dixon	Research Secretary	Nancy.Dixon5@va.gov
Hayley White	Human Research Protection Program Coordinator	Hayley.White2@va.gov
Margaret Jones	Research Compliance Officer	Margaret.Jones@va.gov
Virginia Rhodes	Research Compliance Officer	Virginia.Rhodes@va.gov
Brad Olson	Administrative Officer for R&D	Bradley.Olson@va.gov
John Whited	Associate Chief of Staff for R&D	John.Whited@va.gov
David Edelman	IRB Chair	David.Edelman@va.gov
Nathan Kimbrel	IRB Co-Chair	Nathan.Kimbrel@va.gov
Miriam Morey	R&DC Co-Chair	morey@geri.duke.edu
Jean Beckham	R&DC Co-Chair	Jean.Beckham@va.gov

2: Determination of Project as Research

Submit **ALL** potential or proposed research to the Research Office. The Institutional Review Board (IRB) reviews each proposal.

The IRB answers the following questions in sequence to determine if an activity is research, human subjects research, exempt, or can be expedited:

1. Is this project **research**?
2. If research, does it involve **human subjects**?
3. If human subjects research, is it **exempt** from IRB review?
4. If it is not exempt, is it eligible for **expedited review**?

1. Is this project research?

Research is a *systematic investigation*, including research development, testing and evaluation, designed to develop or contribute to *generalizable knowledge*.

- A systematic investigation is a project that is planned in advance and that uses data collection and analysis to answer a question.
- Generalizable knowledge is information that expands scientific understanding or the knowledge base of a scholarly field of study.

Certain design characteristics are almost always associated with research, such as:

- Double blind interventions
- Use of placebo controls
- Prospective patient-level randomization to clinical interventions not tailored to individual patient benefit

Other design characteristics are often associated with research but may also be used in non-research operations activities, such as:

- Prospective randomization to treatment interventions
- Prospective comparisons of clinical interventions
- Prospective designation of matched pairs
- Interventions with patients to collect clinical information that is not medically necessary

An activity is always research if:

- Funded or supported as research
- Clinical Investigation as defined by FDA

An activity is not research if (See Operations Activities vs. Research section):

- Designed solely for VA's internal purposes, and
- Is not designed to be generalized beyond VA (i.e., not designed to expand scientific understanding or knowledge of base of a scholarly field of study)

2. Does the research involve human subjects?
Human subject means a living individual about whom an investigator conducting research obtains:

- Data through intervention or interaction with the individual, or
- Identifiable private information

Private information must be individually identifiable to constitute research involving human subjects (identity of the subject is or may readily be ascertained by the investigator or associated with the information).

Private information/specimens are not individually identifiable if …

- They are not collected specifically for the currently proposed research; **-AND-**
- Investigators cannot *readily* ascertain the identity of the individuals to whom the coded private information/specimens pertain because of prohibitions to release of the key to the code (e.g., agreement, IRB-approved policy, legal requirements)

3. If it is human subjects research, is it exempt from IRB review?
Research activities in which the only involvement of human subjects will be in one or more of the categories outlined in 38 CFR 16.101(b) may be exempt from the provisions of the Common Rule (Title 38 CFR part 16):

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
(i) research on regular and special education instructional strategies, or
(ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
(i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
(ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
(i) human subjects are elected or appointed public officials or public office candidates; or
(ii) Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research/thereafter.

(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects.

(5) Research and demonstration projects which are conducted by or subject to the approval of Department or Agency head which are designed to study, evaluate, or otherwise examine:

(i) Public benefit or service programs;
(ii) procedures for obtaining benefits or services under those programs;
(iii) possible changes in or alternatives to those programs or procedures; or
(iv) possible changes in methods or levels of payment for benefits or services under those programs.

(6) Taste and food quality evaluation and consumer acceptance studies,
(i) if wholesome foods without additives are consumed or
(ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the EPA or the Food Safety and Inspection Service of the USDA.

4. Can human subject research be reviewed by an expedited process?
1. Must fit one or more of the expedited review categories and be no more than minimal risk
-OR-
2. Minor changes in previously IRB approved research during the period for which the approval is authorized.

Note: Expedited review is a *process* that allows certain types of research protocols (initial and continuing review) and changes to protocols (amendments) to be reviewed outside of an IRB meeting by one or more experienced IRB members. Expedited review does not describe the speed at which a protocol or submission is reviewed, although the ability to review outside of a convened IRB meeting may reduce turn-around time.

Minimal Risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological tests [38 CFR 16.102(i)].

Cannot expedite when identification of the subjects or their responses would reasonably:
- Place them at risk of criminal or civil liability, be damaging to the subjects' financial standing, employability, insurability, or reputation, or be stigmatizing…
- UNLESS reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal

If expedited, the IRB must apply the standard requirements for informed consent (or its waiver, alteration, or exception) to all studies that undergo expedited review.

3. Operations Activities vs. Research

Operations activities are certain administrative, financial, legal, quality assurance, quality improvement, and public health endeavors that are necessary to support VHA's missions of delivering health care to the Nation's Veterans, conducting research and development, performing medical education, and contributing to national emergency response. Operations activities may or may not constitute research.

Research is a systematic investigation (including research development, testing, and evaluation) designed to develop or contribute to generalizable knowledge. Thus, research may be defined as a systematic investigation designed to produce information to expand the knowledge base of a scientific discipline (or other scholarly field of study). ***NOTE:*** *Research typically involves the testing of concepts by the scientific method of formulating a hypothesis or research question, systematically collecting and recording relevant data, and interpreting the results in terms of the hypothesis or question to expand the knowledge base of a field of study. Purely clinical use of an FDA-approved medication or product for an unlabeled indication is not considered research. (However, VA may require informed consent for treatment if safety and efficacy have not been established. If in doubt, providers must contact Pharmacy Benefits Management (PBM) for guidance.)*

A **systematic investigation** is an activity that is planned in advance and that uses data collection and analysis to answer a question. Although research must include systematic investigation, non-research operations activities also include systematic investigation to ensure reliable outcomes. Systematic investigation does not, in and of itself, define research. ***NOTE:*** *Examples of systematic investigations that may or may not constitute research, include (but are not limited to) activities involving questionnaires or surveys; observations; focus groups; interviews; analyses of existing data; analyses of biological specimens; medical chart reviews; epidemiologic reviews or analyses; program evaluations; and quality assessment, quality improvement, and quality management.*

Generalizable knowledge is information that expands the knowledge base of a scientific discipline or other scholarly field of study. Systematic investigations designed to develop or contribute to generalizable knowledge constitute research. Thus, systematic investigations designed to produce information to expand the knowledge base of a scientific discipline or other scholarly field of study constitute research.

Non-Research Operations Activities are activities that are not designed to produce information that expands the knowledge base of a scientific discipline (or other scholarly field) do not constitute research. Thus, a VHA operations activity does not constitute research if both of the following criteria are satisfied:

(1) The activity is designed and implemented for internal VA purposes (i.e., its findings are intended to be used by and within VA or by entities responsible for overseeing VA, such as Congress or the Office of Management and Budget); and
(2) The activity is not designed to produce information that expands the knowledge base of a scientific discipline (or other scholarly field).

Contact the Research Office if you have specific questions as to whether or not an activity constitutes research. In addition, the following table has been designed to assist you in determining whether or not an activity is research.

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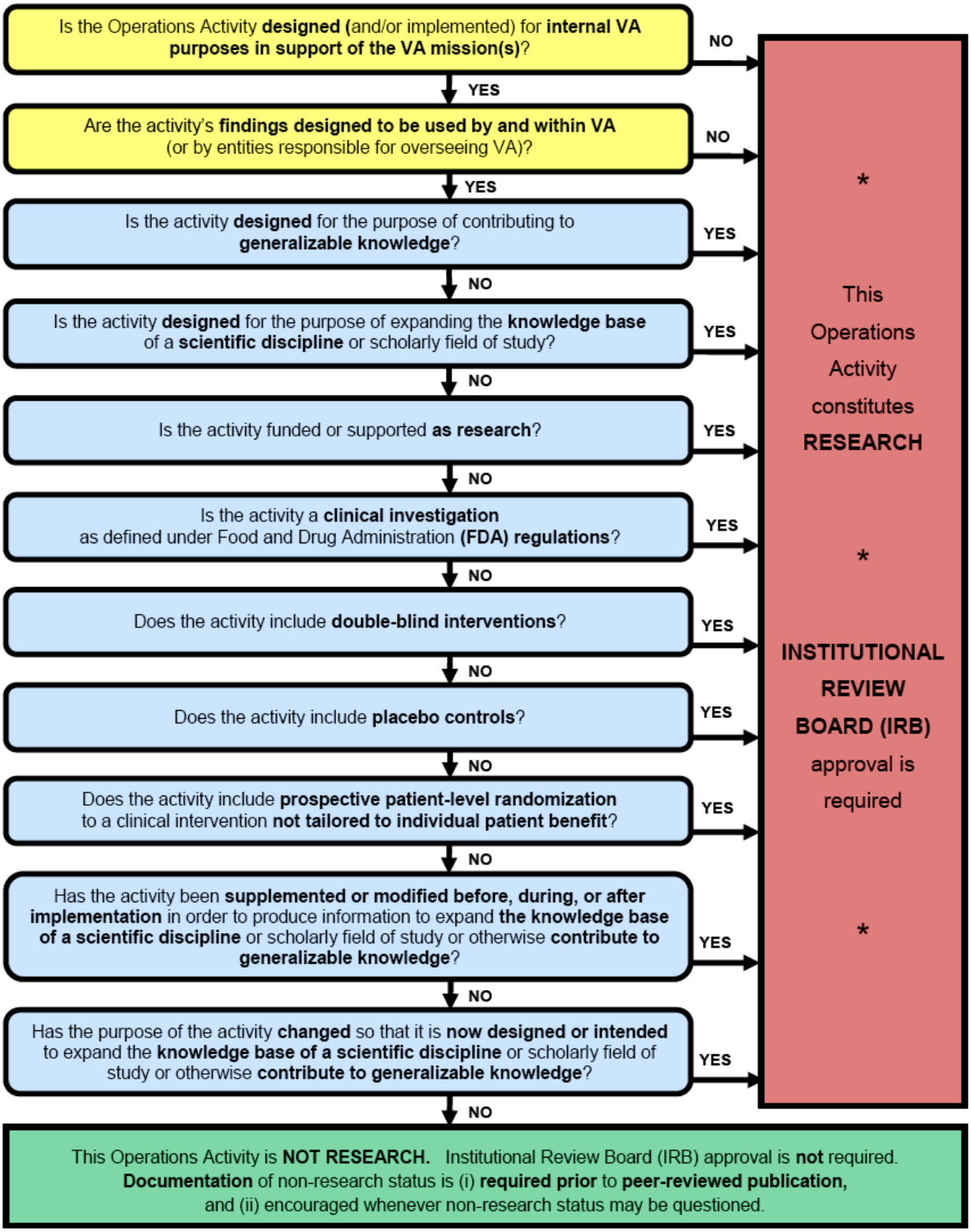
VHA Operations Activities that May Constitute Research



4: Research Training/Personnel Documentation

SOP: GA 102, Research Required Training, Education, and Other Research Personnel Documentation

Website location for forms:
http://www.durham.va.gov/research/amendments/Amendments_Miscellaneous_Forms.asp

A. Required Training

- You must complete all mandatory Durham VAMC training to comply with facility requirements.

- All research training must be complete prior to beginning any research activity.
  - Collaborative Institutional Training Initiatives (CITI) Good Clinical Practice (GCP): required every three years
  - Other research-specific training, as required.

- Submit training documentation to the Research Office, either with an initial submission or when your CITI training is renewed.

B. Required Documentation

1. Research Scope of Practice

- Each member of the Durham VAMC research team (clinical or non-clinical) must have a research scope of practice (SOP) that defines the duties in which the person is trained, qualified, and allowed to perform for research purposes.

- The scope of practice must be signed by the individual, the individual's supervisor, each Principal Investigator (PI) that the individual works with, and the ACOS/R&D.

- You are only authorized to perform the research duties/functions which are listed in your Research Scope of Practice.

- If an employee has a current Research SOP but is assigned to work with a PI that is not listed on the current Research SOP or no longer works with a listed PI, the individual must complete a SOP PI Update Form and submit the form to the Research Office.

- If research duties or responsibilities change during the course of a year, the individual must submit a new SOP with the individual's signature, the supervisor's signature, and all applicable PI signatures for ACOS/R&D signature.

- Submit your Research Scope of Practice to Kim Clark in the Research Office.

2. Staff Listing

- The PI must maintain a Staff Listing for each study for which s/he has responsibility.
- The Staff Listing provides a list of all personnel who conduct any part of the research endeavor and must include the names of all individuals either involved in the conduct of the study or who make decision regarding study procedures.
- For individuals with a Durham VAMC appointment who are involved in the conduct of the study, the Staff Listing also provides the completion dates of CITI GCP training. The presence of a research Scope of Practice is also documented on the Staff Listing.
- A Staff Listing is required at initial review, continuing review, and anytime there is a change to Durham VAMC appointees.
- The PI should keep all Staff Listings and training records of staff members with their specific protocol files.

C. Credentialing and Privileging

- The employee (paid, WOC, or IPA) must have all required licenses, registrations, or certifications to perform a given procedure, intervention, or other activity in the research setting and practice only within the scope allowed by such licenses, registrations, or certifications.
- All VA research staff (clinical and non-clinical) conducting human research (exempt or non-exempt) must be credentialed and privileged (if applicable) as required by current local, VA, VHA (see VHA Handbook 1100.19), and ORD requirements.
- Research staff (including volunteers) may only perform those activities in a research study for which they have the relevant credentials and privileges.

5: Investigator Responsibilities

SOP: RI 801, Investigator Responsibilities

The Investigator is responsible for personally conducting and supervising all study-related activities. The Investigator is ultimately responsible for the conduct of the trial and all actions of the study team. The Investigator is responsible for the following:

- Disclosing conflicts of interest
- Ensuring adequate resources
- Promptly reporting changes in Principal Investigator (PI) or Local Site Investigator (LSI)
- Overseeing research staff
- Ensuring qualified research staff
- Ensuring complete information in research protocols
- Obtaining written approvals (IRB, R&DC, ACOS/R&D)
- Implementing the study as approved
- Obtaining informed consent
- Ensuring consistency of informed consent form, protocol, and HIPAA authorization (VA Form 10-0493)
- Ensuring HIPAA authorization (VA Form 10-0493) is obtained
- Documenting research and consent processes in the medical and research record
- Maintaining Investigator's Research Records
- Maintaining a Master List of all subjects:
    - The Investigator must maintain a master list of all subjects from whom informed consent has been obtained whether or not IRB granted a waiver of documentation of informed consent.
    - Investigators must not add a subject's name to the master list of subjects until after:
        - Informed consent has been obtained from that subject,
        - When appropriate, informed consent has been documented using an IRB-approved consent form.
    - The Investigator must secure the master list in compliance with all VA confidentiality and information security requirements.

      Note: The IRB may waive the requirement for the Investigator to maintain a master list for a given study if both of the following conditions are met: there is a waiver of documentation of informed consent and the IRB determines that including the subjects on such a master list poses a potential risk to the subjects from a breach of confidentiality.
- Ensuring appropriate telephone contact with subjects
    - See requirements for initial and later contact
- Obtaining IRB approval for all changes
- Submitting Continuing Review materials
- Reporting deviations and complaints
- Reporting unanticipated problems and SAEs
- Completing appropriate actions at research project completion
- Transferring records appropriately
- Ensuring appropriate research laboratory test reporting
- Ensuring requirements of multi-site studies

6: IRB Submissions and Reviews: Initial, Continuing, and Amendments

1. Initial Review

SOP: RR 402, Initial Review: Criteria for Approval

Website location for forms:
http://www.durham.va.gov/research/initial_review/Initial_Review.asp

These forms must be completed for initial review submissions (taken from IRB Submission Checklist):

- **Investigator Data/Page 18 (VA Form 10-5368):** Investigator Data/Page 18 is required for new Principal Investigators (PIs) or Co-Investigators only. If the PI has submitted Investigator Data/Page 18 for a prior study, do not re-submit. PIs must be FA faculty (full time, part time, or WOC). Medical residents, fellows, pharmacy students, and nursing students must contact the Research Office prior to a protocol submission.
    - A VA Investigator sufficiently experienced in the area of the trainee's research interest must serve as PI or co-PI and is responsible for oversight of the research and the trainee. The PI or co-PI is responsible for ensuring the trainee complies with all applicable local, VA and other federal requirements.

- **Request to Review / Investigator Overview:** Funding source must be included (write 4 digit number and sponsor name). Once funded, you must notify the Research Office. This form must be signed by the Section/Service Chief or it will not be submitted to the IRB for review. Complete all applicable items.

- **Abstract:** The abstract is mandatory. Abstracts should only be one page long with no special characters. The abstract should include the Purpose, Methodology, and Objectives.

- **Protocol:** The protocol must contain all elements as required in the Research SOP RI 802, Research Protocol. Note: Two protocols may need to be submitted—the main protocol and a local protocol that is Durham specific for the procedures/research that will be done at the Durham VAMC as part of the study.

- **Grant Application:** If applicable, a copy of the grant must be submitted regardless of funding source.

- **Informed Consent:** If applicable, the informed consent form should be drafted using the Durham VA Informed Consent template and must contain elements of informed consent as required in the Research SOP IC 701, General Requirements and Documentation of Informed Consent. If requesting a waiver of documented informed consent, submit the "Waiver of Informed Consent Documentation" form. If requesting a waiver of consent, include a "Waiver or Alteration of Informed Consent Process."

- **HIPAA Authorization (VA Form 10-0493):** You must include a HIPAA authorization form (VA Form 10-0493) or a "Waiver or Alteration of HIPAA Authorization."

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- **Screening/Recruiting:** Most studies will pre-screen potential participants (either by using clinic data, data from CPRS/VistA, etc.). If you wish to do screen and recruit by looking at patient records before getting the patient's informed consent and HIPAA authorization (VA Form 10-0493), you must have a waiver of informed consent to screen and recruit and a waiver of HIPAA authorization to screen and recruit.

- **Include the following as applicable:**
  - Investigator's Brochure, package insert, Form 10-9012 (required for drug studies), all questionnaires that will be given to subjects for completion, typed telephone script, recruitment letters (no drafts), and advertisements (flyers, radio or newspaper adds, etc.)

- **Staff Listing:** A completed Staff Listing must be submitted for initial review.

- **Conflict of Interest (COI) Survey:** All Investigators (including Co- and Sub-Investigators) must complete this form and must obtain signature from the Principal Investigator. The COI survey must also be updated if there are any COI changes during the course of the study.

- **Privacy, Confidentiality, and Information Security Checklist:** The Privacy Officer and Information Security Officer reviews should occur **prior** to IRB submission. Submit the checklist and all required documents electronically to the Privacy Officer and Information Security Officer. **Do not** submit your application to the IRB until you have made all corrections and have signed PO and ISO approval.

- **Data Management and Access Plan (DMAP):** Describes how, where, and to what extent data and results available to the public.

- **Application to Establish a Research Data Repository:** Submit if you wish to create a new Research Data Repository.

- **Application to Use Data from a Data Repository:** Submit if you wish to use data from a data repository.

- **May Also Need the Following:**
  - VA Form 10-0398: Research Protocol Safety Survey, Standard Operating Procedure (SOP) for Using Human Blood or Tissue, Recombinant DNA Form, Viral Vector Form, Training Documentation to Pack/Ship Biological Specimens, Department of Defense (DoD) forms, or Department of Education (ED) forms.

2. Continuing Review

SOP: RR 404, Continuing Review: Criteria for Renewal

Website location for forms:
http://www.durham.va.gov/research/continuing_review/Continuing_Review.asp

Complete the "Request for Continuing Review of Research" form. The following data must be provided at Continuing Review (CR):

- Research Project Status
- Risks/Procedures
- Informed Consent Process
- Enrollment Data
- Serious Adverse Event/Adverse Event/Protocol Deviation Reporting
- Descriptive Summary of Research
- Findings to Date
- Publications (remember to credit the VA in any publications!)
- Conflict of Interest update

3. Amendments

SOP: RR 403, Continuing Review: Ongoing

Website location for forms:
http://www.durham.va.gov/research/amendments/Amendments_Miscellaneous_Forms.asp

Changes in approved research may not be initiated without prior IRB review and approval (full or expedited review, as appropriate), except where necessary to eliminate apparent immediate hazards to human subjects.

All proposed protocol modifications/amendments, changes to consent forms (including proposed plans to re-consent), advertisements, recruitment material, questionnaires, Investigator Brochure or package inserts, changes in study personnel, and change in study status (e.g., premature completion of the study) must be reported to the IRB. The IRB will determine whether changes to the research activities require a change to the Informed Consent document and therefore warrant consideration for re-consenting of currently enrolled participants, or whether participants should be notified of significant new information that might affect their willingness to continue participation, or whether notification of participants who have completed interventions is warranted.

The date of continuing review is not changed based on the approval date of the amendment unless the IRB specifies that the date of continuing review is changed.

Submit a completed *Protocol Amendment IRB Submission Form* (received with initial approval documentation from IRB) plus a separate cover letter describing the change(s) and all appropriate documentation (e.g., revised protocol, consent, 10-9012, etc.) with the request to review.

7: Reportable Events: Adverse Events, Problems, Deviations, Noncompliance

SOP: RR 403, Continuing Review: Ongoing

Website location for forms:
http://www.durham.va.gov/research/amendments/Amendments_Miscellaneous_Forms.asp

Serious Unanticipated Adverse Events, Problems, and Noncompliance

Definitions:
Adverse Event: an undesirable and unintended, although not necessarily unexpected, result arising during the course of a research protocol (*e.g.*, abnormal physical exam or laboratory finding, headache following spinal tap or intestinal bleeding associated with aspirin therapy). VA's definition: An AE is any untoward physical or psychological occurrence in a human subject participating in research. An AE can be any unfavorable or unintended event, including abnormal laboratory finding, symptom, or disease associated with the research or the use of a medical investigation test article. An AE does not necessarily have to have a causal relationship with the research, or any risk associated with the research or the research intervention, or the assessment.

Serious Adverse Event: any adverse event that results in any of the following outcomes: (1) Death, (2) a life-threatening event (that places the subject at immediate risk of death from the event as it occurred), (3) inpatient hospitalization or prolongation of existing hospitalization, (4) a persistent or significant disability/incapacity, or (5) a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Unanticipated (Unexpected): the terms "unanticipated" and "unexpected" refer to an event or problem in VA research that is new or greater than previously known in terms of nature, severity, or frequency, given the procedures described in protocol-related documents and the characteristics of the study population.

Protocol Deviation: any departure, alteration, or procedural error in the IRB approved protocol and/or study procedures that occurs without prior IRB notification and approval. The cause of the deviation may be within the Investigator's control (e.g., change a protocol procedure or medication), or a deviation may not be in the control of the Investigator (e.g., a subject fails to show-up for a procedure defined in the protocol).

Noncompliance: failure to adhere to the local or federal laws, regulations, or policies governing human research.

Serious Noncompliance: failure to adhere to the laws, regulations, or policies governing human research that might reasonably be regarded as involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research participants, research staff, or others; or substantively compromising the effectiveness of a VA facility's human research protection or human research oversight programs.

Continuing Noncompliance: persistent failure to adhere to the laws, regulations, or policies governing human research.

Serious Unanticipated Problems Involving Risk to Subjects or Others:

1) Interruptions of subject enrollments or other research activities due to concerns about the safety, rights, or welfare of human research subjects, research staff, or others.
2) Any work-related injury to personnel involved in human research, or any research-related injury to any other person, that requires more than minor medical intervention (i.e., basic first aid), requires extended surveillance of the affected individual(s), or leads to serious complications or death.
3) Any VA National Pharmacy Benefits Management (PBM) Bulletins or Communications (sometimes referred to as PBM Safety Alerts) relevant to one or more of the facility's research projects.
4) Any Data Monitoring Committee (DMC), Data Safety Monitoring Board (DSMB), or Data Safety Monitoring Committee (DSMC) report describing a safety problem.
5) Any sponsor analysis describing a safety problem for which action at the facility level may be warranted. Sponsor "AE Reports" lacking meaningful analysis are not considered problems.
6) Any unanticipated problem involving substantive harm, or a genuine risk of substantive harm, to the safety, rights, or welfare of human research subjects, research staff, or others.
7) Any problem reflecting a deficiency that substantively compromises the effectiveness of a facility's human research protection or human research oversight problem.
8) Any protocol deviation that places one or more subjects at increased risk of harm.
9) Any lost or stolen electronic devices used in or for research purposes (laptop computers, personal digital assistants or other electronic recording devices, etc.)
10) Other incidents that involve risks to subjects or others may also be serious unanticipated problems.

Reporting:

1. Within **one hour** of becoming aware of any unauthorized use, disclosure, transmission, removal, theft, loss or destruction of VA-related protected health information (PHI), individually identifiable private information, or confidential information, (as defined by the HIPAA Privacy Rule, the Common Rule, the Privacy Act, or 38 U.S.C. §5701, 5705, and 7332), report event to the ACOS/R&D, the ISO, and the PO. The use of this e-mail address will ensure that such notifications are sent to the ACOS/R&D, ISO, PO, and other research personnel: VHADURResearchEventReport@va.gov

    - Complete the **Report Form for Privacy and/or Information Security Incidents in VA Research** within 5 business days of becoming aware of any local Information Security or Privacy Incident related to a VA Research study.

2. Within **5 business days** of becoming aware of any **local Serious Unanticipated Problem** or **local Unanticipated Serious Adverse Event** determined to be **related to the research**. For SAEs and Unanticipated Problems, report via a **Serious Unanticipated Adverse Event or Problem Related to Research Form**.

3. If SAE, AE, problem, or deviation is anticipated, (i.e., documented in the protocol or consent and expected for study population), or unanticipated and not related to research report at **Continuing Review**.

See the current "Local Event Reporting Guidance" flowchart for reference.

8: Required Documentation

SOP: RI 801: Investigator Responsibilities

Record Retention: All research records will be maintained and destroyed in accordance to VHA RCS 10-1. Contact research office for record retention requirements.

You must keep detailed research records/binders/files. Keep all of the following:

- Copies of all IRB-approved versions of the protocol and amendments
- Case report forms and supporting data, including, but not limited to, signed and dated informed consent forms and HIPAA authorizations (VA Form 10-0493)
- Documentation on each subject including, but not limited to:
  - informed consent
  - interactions with subjects by telephone or in person
  - observations
  - interventions
  - progress notes
  - research study forms
  - surveys
  - questionnaires
- Reports of adverse events
- Data analyses
- Reports including, but not limited to, abstracts and other publications
- All correspondence including, but not limited to, correspondence with the funding source or sponsor and with applicable oversight entities including, but not limited to the IRB, R&DC, ORO, and FDA

Source Documents: Source documents are documents in which research data are first recorded and may include CPRS notes, lab reports, x-rays, questionnaires, surveys, etc. Subject source documents **must** contain the following:

- Verification that subject met all of the inclusion criteria and none of the exclusion criteria
- Documentation of all Serious Adverse Events (SAEs) and serious problems
- Evidence that informed consent was obtained prior to beginning study procedures

Helpful Hints:

- Create a log and document when you submit an item to the IRB and when you receive a response from the IRB
- Time stamp all submissions to the IRB and make a copy of the time-stamped document for your records
- Follow-up if you do not receive correspondence in a timely fashion
- Carefully read correspondence from the IRB: If something is wrong or missing from an approval letter, notify the IRB to get the mistake corrected
- Review consent forms, protocols, etc. for IRB approval date stamps

- Use notes-to-file to describe any unusual study procedures or explain anything that may be confusing to an outside observer. Note that notes-to-file are not the same as protocol deviation reports.

9: Informed Consent / Consent Documentation / HIPAA

SOPs:

- IC 701: General Requirements and Documentation of Informed Consent
- IC 702: Waiver of Informed Consent
- IC 703: Surrogate Consent and Assent
- IC 704: Privacy Rule and Research
- RI 803: Research Records and Documentation of Research

Website location for forms:
http://www.durham.va.gov/research/initial_review/Initial_Review.asp
http://www.durham.va.gov/research/amendments/Amendments_Miscellaneous_Forms.asp
http://www.durham.va.gov/research/Privacy_Info_Sec/Privacy_Information_Security.asp

1. Informed Consent

- Informed consent is a *process* where the potential subject becomes informed about the research and makes a thoughtful determination to participate, continue participation, or decline participation in a research study. It is not just a document to be signed.

- In general, all prospective studies require written informed consent documents (ICD) signed and dated by the subject and the person obtaining informed consent.

- See SOP IC 701 for requirements of the informed consent form (ICF).
    - ICFs have very detailed requirements! Contact HRPP Coordinator or Research Office with questions related to the informed consent document.

- Documentation of informed consent:
    - Keep the original signed and dated consent form (and HIPAA authorization (VA Form 10-0493), if separate); provide a copy of the signed document(s) to the subject.

    - Research Consent Note in CPRS: Within 24 hours of the subject signing the consent form, the person who provided the consent process must enter a Research Consent Note into CPRS.
        - If a non-veteran is entered into a VA research study, those consents are usually not entered into CPRS, rather keep a paper research record and include documentation of the consent process in the file.
        - If the study has a waiver of documented informed consent, the person who provided the consent process must enter a Research Consent Note in CPRS. The note must document the process by which consent was obtained in the 'Other' section of the research consent note template (e.g., waiver of documented consent). The research consent note is not required if the waiver was approved secondary to a potential breach of confidentiality.

- Research Study Participant Note (Clinical Warning): If required by the IRB, enter a Research Study Participant Note (Clinical Warning) in CPRS within 24 hours of the veteran signing the consent. This note will need to be removed once study participation is complete.
  - If applicable, scan the Form 10-9012 (Investigational Drug Information Record) and attach to the Research Study Participant Note as soon as possible but no later than 14 days after the subject signs consent.
  - If the subject is a non-veteran, ensure that Pharmacy receives a paper copy of the subject's 10-9012 and signed informed consent form and HIPAA authorization (VA Form 10-0493).

2. Waiver of Documentation of Informed Consent

- Consent process occurs but the subject does not sign a written consent form.
- You must request and receive approval from the IRB for a waiver of documented consent; you must also apply for a HIPAA waiver of authorization.
- Consent process may be verbal or evidenced by the fact that the subject returned a mailed questionnaire, etc.
- IRB may require PI to provide the subject with a written statement regarding the research.
- Unless the IRB approved the request for waiver of documented informed consent secondary to a potential breach of confidentiality, you must document the consent process in CPRS via a Research Consent Note.
- Criteria for Waiver of Documentation of Informed consent are as follows:
  - The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; **or**
  - That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

3. **Waiver of Informed Consent**

- Only applicable for non-FDA regulated minimal risk research.
- No consent process occurs.
- You must request and receive approval from the IRB to waive the informed consent process; you must also apply for a HIPAA waiver of authorization.
- Criteria for Waiver of Informed Consent in Minimal Risk Research are as follows:
  - Research involves no more than minimal risk to the subjects; **and**
  - Waiver or alteration will not adversely affect the rights and welfare of the subjects; **and**

- Research could not practicably be carried out without the waiver or alteration; **and**
- Whenever appropriate, the subjects are provided with additional pertinent information after participation.

4. HIPAA (Health Insurance Portability and Accountability Act)

- The VHA takes data privacy (and data security) very seriously and adheres to the Privacy Act of 1974, Title 38 requirements, and the HIPAA Privacy Rule.

- There is a difference between requesting a HIPAA waiver to screen and recruit and a HIPAA waiver to screen, recruit, and conduct the study. Both scenarios require the Investigator to complete a "Waiver or Alteration of HIPAA Authorization."

10: Research Audits

Reference: VAMC Memorandum 558-14-00.24: Research Compliance Program

All research will receive regular audits. Audits are not meant to be punitive, rather they are a chance for the Investigator and Research Compliance Officer (RCO) to review research records and ensure that research policies were followed during the conduct of the research. Audits are educational and collaborative.

1. Informed Consent Audits

- The VHA requires annual informed consent audits on 100% of all signed consent forms (and HIPAA authorizations, if separate).

- A final ICF audit will be conducted at the time of study closure with the IRB.

- The RCO will request the following prior to an ICF audit:
  - A list of names of individuals who have signed consent in the past year
  - Unique subject identifier for each individual who signed consent in the past year
  - Last four digits of each subject's SSN
  - Date consent was signed
    - If this list is provided to the RCO electronically, you must use PKI to transmit the information. Hard copies of the list may be delivered to the RCO, or, if very few subjects were consented, this information may also be conveyed via a phone call to the RCO.

  - Note: If you maintain this list throughout the study, it could also serve as your master list of subjects.

- The RCO will conduct the audit, discuss the results with the PI and/or Coordinator, draft an audit report, and share the report with the PI and the IRB.

- The IRB will provide a letter to the PI with any recommendations.

2. Regulatory Audits

- The VHA requires triennial regulatory audits for any study opened after January 2008.
- If a study is active less than three years before study closure, the study will receive a regulatory audit at the time of study closure with the IRB.
- The RCO will review the following documents as applicable:
  - R&D, IRB, and SRS initial approval letters
  - Approved protocol and amendments/modifications
  - Approval letters for amendments/modifications
  - Annual continuing review approval from the IRB and SRS
  - IRB approved ICF (current and archived)
  - Investigator Brochure and FDA Form 1572 (as applicable)
  - Pharmacy accountability documentation and VA Form 10-9012 (as applicable)
  - Study Staff Listing (current and archived)
  - Scope of Practice documents
  - Documentation of research-required training (CITI)
  - Completed VA Form 10-0398 (Appendix G) and any SRS-required SOPs

In addition, the RCO may review source documents for select participants.

- The RCO will conduct the audit, discuss the results with the PI and/or Coordinator, draft an audit report, and share the report with the PI and the IRB.
- The IRB will provide a letter to the PI with any recommendations.

3. For-Cause Audits

- For-Cause audits may be authorized/requested by the IRB for various reasons.
- If your research is selected for a for-cause audit, you will be notified and given instructions as to what documentation will be reviewed.

4. Preparing for an Audit

- Maintaining good research records throughout the conduct of the study is the key to a successful audit.
- Provide/have available are required documentation.
- Keep calm and carry on.

11. Study Closure

SOP: RR 405, Study Completion

How do I know when I can close a study?

Studies may be closed when:

- Individually identifiable data are no longer being collected,
- All approved data analyses (and manuscript preparations) are complete,
- The sponsor closes a study or, if multi-site industry-sponsored research, the PI submits a final report to the sponsor, or
- Multi-site non-industry studies where Durham is not the lead site may be closed with the Durham PI is no longer collecting data, or

- Other circumstantial reasons.

How do I close a study?
Investigators must submit a notice of study termination in the form of a memorandum along with a progress report and information of subject experiences to the Research office. Although subjects will no longer be "at risk" under the study, the final report/notice provides information that may be used by the IRB in the evaluation and approval of related studies.

Studies may also be closed at the time of continuing review. Indicate on the continuing review application that the study is complete and you wish to administratively close the files (Question 1, option f). Complete the rest of the continuing review form and submit the progress report.

Note that if the research is being conducted by a trainee (medical or pharmacy resident or fellow, etc.) and the trainee does not complete all aspects of the research prior to leaving VA, the VA employee serving as the PI or co-PI must ensure the protocol is completed and closed per requirements. The PI or co-PI is also responsible for ensuring all research records are retained by VA.

If a study is closed, what can we do with the data?
It depends.

- If data are identifiable: Store data, per VHA Records Control Schedule (contact the Research Office for more information on the VHA RCS). No further data analyses may be conducted.

- If data are de-identified: Open a research study with the R&D Committee (via an IRB exemption) to analyze data (see below).

Is there a way we can be forward thinking in designing consent forms, etc., so that the original study can be closed, but the data (maybe de-identified data) can still be used in the future without re-opening the study?
Add opt-in/opt-out statement(s) such as:

"I give permission for data collected from this study to be used for {*future research studying the same disease as the current study / future research to study any condition / other qualifying statement*}." You must also state where the data will be stored and who will have access to the data.

Each statement must have yes/no option and data fields for the date and subject initials.

Note that there must be a data repository protocol if you store data for future use.

What if an investigator would like to initiate a research project using identifiable data from a closed study?
An investigator may submit a new research application to initiate research using identifiable data from a closed study. The new research application should reference the closed study's database.

The IRB will review the request and will need to review the protocol/ICF/HIPAA from the previous study to ascertain 1) whether the proposed research is in the scope of the previous research, and 2) whether the previous study's protocol/ICF/HIPAA will allow future use.

There is no guarantee that you will be able to use identifiable data from a previous study.

What if an investigator would like to initiate a research project using de-identified data? Unless FDA regulated, the Durham VAMC IRB does not need to review research with de-identified data, as it is not human subject research.

However, it's still research, and the VA requires oversight of all research activities.

To use de-identified data, submit an Exemption Application to the IRB, and if the IRB agrees the research is exempt, the Research Office will forward the study application for R&DC review. Note that the research will still require continuing review by the R&DC.

12. Publication or Presentation of Research and Non-Research Results

Research Publications or Presentations

1) Acknowledge VA research support and/or VA employment in all publications, presentations, media interviews, or professional activity where research results are being publicized, presented, recognized, or discussed.

2) Submit copies of publications and summaries of presentations as part of the IRB continuing review (or study closure) process.

3) Follow the Office of Research and Development's (ORD) current guidelines for submitting publications or presentations of original research, commentaries, review articles, letters to the editor, and other journal publications to ORD's PubTracker prior to publication or presentation.

Non-Research Publications or Presentations

Publication or presentation outside VA of findings from non-research operations activities or other non-research activities does not, in and of itself, constitute research. Contact the Research Office with any questions.

Program Office Peer-Reviewed Publications: Publication in peer-reviewed journals (including electronic peer-reviewed journals) of findings from non-research activities that were funded, mandated, managed, sponsored, or otherwise supported by a VHA Program Office, or that utilized Program Office data, requires documentation of the non-research status of the activities by the relevant Program Office prior to publication.

Other Peer-Reviewed Publications: Publication in peer-reviewed journals (including electronic peer-reviewed journals) of findings from non-research activities requires documentation, prior to publication, of the non-research status of the activities by the lead VA author's Network Director (for Network operations activities) or Facility Director (for facility operations activities), or other individual designated in writing by the Network or Facility Director.

Documentation Content: Documentation content is documentation for peer-reviewed publications based on non-research activities and must include:

- A copy of the manuscript to be published, including the name and VA duty station or institutional affiliation of each author and coauthor.
- An attestation, signed by each VA author or co-author, that the reported findings were not derived, in whole or in part, from activities constituting research.
- The signature of the documenting official. ***NOTE:*** *A sample format for documentation of non-research activities is provided on ORO's Web site at www.va.gov/oro/.*
- Each VA author and coauthor must retain a copy of the documentation for a minimum of 5 years after publication and in accordance with any applicable records retention schedules.

Other Program Office Publications or Presentations: Other than peer-reviewed publications, publication, presentation, or dissemination of findings from non-research activities that were funded, mandated, managed, sponsored, or otherwise supported by a VHA Program Office, or that utilized Program Office data, is subject to the requirements of the relevant Program Office.

Other Publications or Presentations: Publication, presentation, or dissemination outside VA of findings from non-research activities is subject to the requirements of the lead VA author's Network or facility, as applicable.